

AD _____

Award Number: DAMD17-02-1-0201

TITLE: The Effects of Total Sleep Deprivation and Recovery Sleep
on Cognitive Performance and Brain Function

PRINCIPAL INVESTIGATOR: J. Christian Gillin, M.D.
Sean P.A. Drummond, Ph.D.
Gregory Brown, Ph.D.

CONTRACTING ORGANIZATION: Veterans Medical Research Foundation
San Diego, California 92161

REPORT DATE: August 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20040220 044

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE August 2003	3. REPORT TYPE AND DATES COVERED Annual (15 Jul 02-15 Jul 03)	
4. TITLE AND SUBTITLE The Effects of Total Sleep Deprivation and Recovery Sleep on Cognitive Performance and Brain Function			5. FUNDING NUMBERS DAMD17-02-1-0201	
6. AUTHOR(S) J. Christian Gillin, M.D. Sean P.A. Drummond, Ph.D. Gregory Brown, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Veterans Medical Research Foundation San Diego, California 92161 E-Mail: jgillin@ucsd.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) An ever-increasing number of military personnel and civilians alike must work daily without adequate sleep. Although considerable data show sleep deprivation alters many aspects of behavior, little is known about changes in the brain substrate underlying the behavioral effects. Even less is known about the cerebral effects of recovery sleep. The objective of this study is to investigate the effects of 2 full nights of sleep loss and 2 full nights of recovery sleep on cognitive performance and brain function. We will study 40 individuals for 6 nights and 6 days. Over the course of this period, subjects will receive 4 polysomnograms and 10 functional magnetic resonance imaging (fMRI) sessions. During the fMRI sessions, functional brain imaging data will be collected while subjects perform each of 3 cognitive tasks: sustained attention, arithmetic working memory, and verbal learning. In addition to these 40 individuals in the sleep deprivation protocol, we will recruit 10 separate individuals who will participate only in the fMRI portion of the protocol, not the sleep or sleep deprivation portions. These data will allow us to determine the effects on fMRI measures of brain activation due to repeated measurements, independent of any sleep or sleep deprivation related effects.				
14. SUBJECT TERMS Sleep deprivation; cognitive function; functional magnetic resonance imaging; recovery sleep; attention; verbal learning; working memory				15. NUMBER OF PAGES 5
				16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

Table of Contents

Cover.....	Page 1.....
SF 298.....	Page 2.....
Table of Contents...	Page 3.....
Introduction...	Page 4.....
Body.....	Pages 4 and 5.....
Key Research Accomplishments...	Page 5.....
Reportable Outcomes...	Page 5.....
Conclusions...	Page 5.....
References....	Page 5.....
Appendices.....	Page 5.....

Introduction:

An ever-increasing number of military personnel and civilians alike must work daily without adequate sleep. Although considerable data show that sleep deprivation alters many aspects of behavior, including motor skills and cognitive performance, little is known about changes in the brain substrate underlying the behavioral effects. Even less is known about the cerebral effects of recovery sleep. The overarching objective of this study is to investigate the effects of 2 full nights of sleep loss and 2 full nights of recovery sleep on cognitive performance and brain function. To accomplish this goal, we will study 40 individuals for 6 nights and 6 days. Over the course of this period, subjects will receive 4 polysomnograms and 10 functional magnetic resonance imaging (fMRI) sessions. During the fMRI sessions, functional brain imaging data will be collected while subjects perform each of 3 cognitive tasks: sustained attention, arithmetic, working memory, and verbal learning. In addition to these 40 individuals in the sleep deprivation protocol, we will recruit 10 separate individuals who will participate only in the fMRI portion of the protocol, not the sleep or sleep deprivation portions (the "Aim 5" portion of the protocol). These data will allow us to determine the effects on fMRI measures of brain activation due to repeated measurements, independent of any sleep or sleep deprivation-related effects.

Body:

During Year 1 of this study, we successfully accomplished all study preparation and set-up procedures. This includes hiring all staff, purchasing major equipment, and developing Standard Operating Procedures. Additionally, we have trained all staff in the multi-disciplinary aspects of this protocol, including subject recruitment and screening, behavioral testing, polysomnography, overnight sleep deprivation monitoring, and functional magnetic resonance imaging data collection and initial processing.

As reported in a letter to the Commander in March 2003, and reflected in a revised Statement of Work submitted to Dr. Sherry Ward in April 2003, we experienced delays in the timeline for enrolling and completing subjects through the protocol. This was due to delays in the opening of UCSD's new Center for Functional Magnetic Resonance Imaging (the "Center"). This facility houses the MRI scanner to be used for the study. In the two months leading up to the scheduled opening of the Center on April 1, 2003, Dr. Drummond (the research team member responsible for SOP development and implementation and day-to-day execution of the study) spent approximately 120 hours preparing and testing the MRI scanners for this study. In March and April 2003, we ran subjects through a shorter sleep deprivation paradigm in final preparations to begin this study. At the end of April 2003, the Center Directors made the decision to return the MRI scanners to the manufacturer. This decision was based on the fact that while, with considerable effort, the MRI scanners provided acceptable data for basic fMRI studies, they were not well suited for UCSD's efforts to advance our cutting edge fMRI research capabilities. Therefore, the manufacturer of the scanners, Varian, will replace them this fall with another vendor's equipment.

Despite the fact that the MRI scanners are being replaced, we were fully ready to enroll subjects in May 2003. This readiness was based on having met all Year 1 goals, and having perfected the logistics of conducting sleep deprivation studies at the Center through our shorter protocol. We thus decided to recruit, enroll, and run two subjects through the entire sleep deprivation protocol for this study. Doing so allowed us to finalize the logistics for this longer protocol, including coordinating subject scheduling, staffing, behavioral testing, and meals at the Laboratory for Sleep and Chronobiology, as well as twice daily fMRI scanning at the Center. These two subjects were completed successfully through the entire sleep deprivation protocol in

the last week of June 2003. In this respect, we were able to surpass the goals of our revised Statement of Work submitted April 2003.

Based on this successful experience, we now plan to continue to enroll subjects into the study. We are able to do this for two reasons. First, the MRI scanners, while not appropriate for long-term needs at UCSD, currently produce publication-quality data. Second, we are collecting the data necessary (e.g., field maps and baseline scans) to allow us to fully combine subject data collected on the existing system with data from the new system, once installed. Thus, we see no need to wait until the new scanners are installed to enroll more subjects.

Research Accomplishments:

- Purchase of all equipment and supplies required to begin the study
- Developed and implemented all Standard Operating Procedures
- Hired all staff and trained them in behavioral methodology, polysomnography, and FMRI methodology
- Set-up and tested FMRI protocols on the new Varian MRI scanner.
- Designed, programmed, and tested all computerized cognitive tasks to be used in the study, as well as tested the interface equipment used to collect behavioral data during the FMRI sessions
- Enrolled and completed two (2) subjects through the sleep deprivation protocol.

Reportable Outcomes:

Sufficient data has not been collected to allow for reportable outcomes.

Conclusions:

We accomplished all stated goals for Year 1 in our April 2003 Statement of Work. While we experienced delays in enrolling subjects in this study due to delays in the opening of the Center for Functional Magnetic Resonance Imaging, we did have two subjects successfully complete the sleep deprivation protocol. We anticipate that we will be able to compensate for the enrollment delay in future years of the study, so that by the end of the project period, we will accomplish all aspects of the Statement of Work within the originally awarded budget.

References:

N/A

Appendices:

None